IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

MICROSPHERIX LLC, Plaintiff, v. MERCK SHARP & DOHME CORP., MERCK SHARP & DOHME B.V. AND ORGANON USA, INC., Defendants.	Civil Action No. 2:17-cv-03984 (CCC/MF) JURY TRIAL DEMANDED FILED UNDER SEAL

DEFENDANTS MERCK SHARP & DOHME CORP., MERCK SHARP & DOHME B.V. AND ORGANON USA, INC.'S
OPENING CLAIM CONSTRUCTION BRIEF

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TABLE OF ABBREVIATIONS

Abbreviation	Definition
'193 Patent	U.S. Patent No. 6,514,193 (filed May 18, 2001) (issued February 4, 2003) (D.I. 1-2)
'402 Patent	U.S. Patent No. 9,636,402 (filed May 13, 2015) (issued May 2, 2017) (D.I. 1-1)
'401 Patent	U.S. Patent No. 9,636,401 (filed August 29, 2014) (issued May 2, 2017) (D.I. 1-3)
'835 Patent	U.S. Patent No. 8,821,835 (filed June 13, 2013) (issued September 2, 2014) (D.I. 1-4)
'310 Patent	U.S. Patent No. 7,776,310 (filed September 19, 2003) (issued August 17, 2010)
'128 Provisional	Provisional Appl. No. 60/249,128 (filed November 16, 2000)
'050 Provisional	Provisional Appl. No. 60/412,050 (filed September 19, 2002)
Asserted Patents	the '402, '401, and '835 Patents
IPR	*Inter Partes* Review
POSA	Person of ordinary skill in the art
Park Decl.	Declaration of Dr. Kinam Park, filed concurrently herewith
Ex.	Exhibit to the Declaration of Andrew P. Blythe, filed concurrently herewith
Prov.	Provisional
Fig.	Figure

Abbreviation	Definition
Grimm	U.S. Patent No. 5,938,583 (filed December 29, 1997) to Grimm (issued August 17, 1999)
Taber	Taber's Cyclopedic Medical Dictionary, 19th edition (2001))
Stedman	Stedman's Medical Dictionary, 27th Edition (2000)
Merriam	Merriam-Webster's Medical Desk Dictionary, Revised Edition (2002)
Webster	Webster's II New College Dictionary (1999)
Dorland	Dorland's Illustrated Medical Dictionary, 30th Edition (2003)
Mosby	Mosby's Medical Dictionary, 6th Edition (2002)
Fraser	"New prospects for luteinizing hormone releasing hormone as a contraceptive and therapeutic agent" by H M Fraser, dated October 9, 1982
'402 FWD	Final Written Decision, IPR2018-00393 (Paper 43), dated July 8, 2019
'401 FWD	Final Written Decision, IPR2018-00402 (Paper 44), dated July 8, 2019
'835 FWD	Final Written Decision, IPR2018-00602 (Paper 43), dated July 8, 2019
PTO	United States Patent and Trademark Office
PTAB	Patent and Trial Appeal Board
MX Ev.	Microspherix's Rebuttal Claim Construction Evidence (served September 1, 2020)

Abbreviation	Definition
1/12/12 Pros. Tr.	Oral argument transcript for the January 12, 2012 hearing before the PTAB from the prosecution file of U.S. Patent Appl. No. 10/852,407
MX Inf. Cont.	Microspherix's Preliminary Disclosure of Asserted Claims and Infringement Contentions Against Defendants (served March 7, 2018)
MX Val. Cont.	Microspherix's Preliminary Responsive Validity Contentions (served June 8, 2018)
SDG Rep.	SDG Report No. 4678, dated October 1996
'401 POR	Patent Owner's Response, IPR2018-00402, Paper 24, dated October 23, 2018
'401 POPR	Patent Owner's Preliminary Response, IPR2018-00402, Paper 8, dated May 7, 2018
'401 FH Srch.	Examiner's Search Strategy and Results, dated April 18, 2016, from the prosecution file of U.S. Patent Appl. No. 14/473,159, which issued as U.S. Patent No. 9,636,401
Kiser Decl.	Declaration of Dr. Patrick F. Kiser, Ph.D. in IPR2018-00402 (Ex. 2001), dated May 7, 2018
'402 POPR	Patent Owner's Preliminary Response, IPR2018-00393 (Paper 6), dated April 10, 2018
'402 POR	Patent Owner's Response, IPR2018-00393 (Paper 24), dated October 23, 2018
'402 POSR	Patent Owner's Sur-Reply, IPR2018-00393 (Paper 34), dated March 5, 2019

Abbreviation	Definition
IPR Hr'g Tr.	Transcript from April 8, 2019 Oral Hearing for IPR2018-00393 ('402 Patent), IPR2018-00402 ('401 Patent), IPR2018-00602 ('835 Patent) (Paper 42 in IPR2018-00393)
MX Hr'g Sl.	Microspherix's Demonstratives for April 8, 2019 Oral Hearing for IPR2018-00393 ('402 Patent), IPR2018-00402 ('401 Patent), IPR2018-00602 ('835 Patent) (Ex. 2153 in IPR2018-00393)

TABLE OF PARTIES' PROPOSED CONSTRUCTIONS

Claim Term	Merck's Proposal	Microspherix's Proposal
"**target tissue**" '401 Patent claims 1–5, 9, 10, 13–16, 18–19, and 25 '835 Patent claims 1, 3, 4, 10, 16, and 20	"the tissue into which the implantation is intended and on which the agent acts to produce its intended effect"	Plain and ordinary meaning, "tissue into which implant is implanted"
"**seed, for implantation into a subject**" '835 Patent claims 1, 3, 4, 10, and 16	"seed, for implantation into a subject at or near the site on which the agent acts to produced its intended effect"	Plain and ordinary meaning, "implant shaped to pass through a needle bore, for implantation into a subject"
"**strand for administration of a therapeutic agent to a subject in need thereof**" '402 Patent claims 6, 9	"strand for administration of a therapeutic agent that acts to produce its intended effect at or near the implantation site in a subject in need thereof"	Plain and ordinary meaning, "elongated implant for administration of a therapeutic agent to a subject in need thereof"
"**strand for implantation into a subject**" '401 Patent claims 1–5, 9, 10, 13–16, and 18–19	"strand for implantation into a subject at or near the site on which the agent acts to produced its intended effect"	Plain and ordinary meaning, "elongated implant for implantation into a subject"
"**therapeutic agent**" '402 Patent claims 6, 9 '401 Patent claims 1–5, 9, 10, 13–16, 18–21, 23–25 '835 Patent claims 1, 3, 4, 10, 16, 17, and 20	"an agent for the treatment of disease"	Plain and ordinary meaning, "agent that exerts a desired medically beneficial or physiological effect"

Claim Term	Merck's Proposal	Microspherix's Proposal
"**prophylactic agent**" '401 Patent claims 1–5, 9, 10, 13–16, 18–21, and 23–25 '835 Patent claims 1, 3, 4, 10, 16, 17, and 20	"an agent for the prevention of disease"	Plain and ordinary meaning, "agent for prevention of an undesired or non-beneficial physiological condition"
"**marker component**" '401 Patent claims 1–5, 9, 10, 13–16, 18–21, and 23–25 '835 Patent claims 1, 3, 4, 10, 16, 17, and 20	"the part of the seed/strand that is a marker"	Plain and ordinary meaning, "component of a device that comprises a marker"
"**hollow interior**" '401 Patent claims 1–5, 9, 10, 13–16, 18–21, and 23–25 '835 Patent claims 1, 3, 4, 10, 16, 17, and 20	"an empty space defined by and inside the wall of the marker component"	Plain and ordinary meaning, "interior space"
"**wherein the agent is disposed within the hollow interior of the tube**" '835 Patent claim 20	"wherein the agent is disposed within the empty space defined by and inside the wall of the marker component"	Plain and ordinary meaning, "where in the agent is disposed within the interior space of the tube"
"**[marker component] . . . having a substantially continuous wall bounding a hollow interior**" '401 Patent claims 1–5, 9, 10, 13–16, and 18–19 '835 Patent claims 1, 3, 4, 10, 16, and 20	The marker component itself constitutes a wall that defines the hollow interior.	Plain and ordinary meaning, "[component of a device that comprises a marker] . . . having a substantially continuous wall bounding a hollow interior"

Claim Term	Merck's Proposal	Microspherix's Proposal
"**[marker component] . . . having a substantially continuous wall along the length, the substantially continuous wall bounding a hollow interior**" '401 Patent claims 20– 21, and 23–25 '835 Patent claim 17	The marker component itself constitutes a wall that defines the hollow interior.	Plain and ordinary meaning, "[component of a device that comprises a marker] . . . having a substantially continuous wall along the length, the substantially continuous wall bounding a hollow interior"
"**polymeric coating**" '402 Patent claims 6, 9	"a layer of polymer that is formed as a result of applying it or building it up to cover the existing surface of the strand/implantable rod"[1]	Plain and ordinary meaning, "a layer of polymer"
"**rod**" '402 Patent claims 6, 9	"a unitary cylinder"	Plain and ordinary meaning, "cylinder-shaped device"
"**flexible**" '401 Patent claims 1–5, 9, 10, 13–16, 18–21, and 23–25	Indefinite Alternatively: "capable of bending"	Not indefinite, plain and ordinary meaning, "not rigid or flaccid"
"**marker**" '401 Patent claims 1–5, 9, 10, 13–16, 18–21, and 23–25	"a substance less toxic than barium sulfate that is added to enhance imageability"	Plain and ordinary meaning, "material included for detection using standard imaging techniques"

[1] Replacing the phrase "to cover" in Merck's proposed construction with "on" would not change the substance of the construction if the Court finds it is a more appropriate construction.

Claim Term	Merck's Proposal	Microspherix's Proposal
'835 Patent claims 1, 3, 4, 10, 16, 17, and 20		
"**radio-opaque material**" '402 Patent claims 6, 9	"a substance less toxic than barium sulfate that can be detected by conventional x-ray imaging techniques"	"material that can be visualized by conventional x-ray imaging"
"**agent . . . selected from the group consisting of . . . radiopaque**" '401 Patent claim 15 '835 Patent claim 16	"a substance less toxic than barium sulfate that can be detected by conventional x-ray imaging techniques"	"agent . . . selected from the group consisting of . . . material that can be visualized by conventional x-ray imaging"
"**radio-opaque**" and "**radiopaque**" '402 Patent claims 6, 9 '401 Patent claim 15 '835 Patent claim 16	"detectable by conventional x-ray imaging techniques"	"capable of visualization by conventional x-ray imaging"

I. INTRODUCTION

Plaintiff and Counter-Claim Defendant Microspherix LLC ("Microspherix") holds patents directed to "brachytherapy." Each Asserted Patent is entitled "Flexible and/or Elastic *Brachytherapy* Seed or Strand," and states at the beginning of the specification: "This application relates to imagable [sic] implantable *brachytherapy* devices, and methods of use thereof." '402 Patent at Title, 1:28-29.[2] As the patents further explain, "brachytherapy" is the treatment of cancerous tissue via targeted, localized delivery of radioactivity directly to the site of the tumor. *Id*. at 1:30-41.

While the specifications of the '402, '401, and '835 Patents (collectively, "Asserted Patents") contemplate extending traditional brachytherapy principles to non-radioactive therapeutics, they never depart from describing—and touting the advantages of—brachytherapy's fundamental hallmark of targeted, *localized* delivery of agents for treating *disease*.[3] As the patents explain, such localized treatment is advantageous because it delivers agents directly *into* the target tissue, and, "[s]ince concentrations of the therapeutically active substance will be greater at the implantation site (e.g., the diseased tissue), any potentially deleterious effect of the therapeutically active substance on healthy tissue located away from the

[2] Citations to the '402 Patent specification also refer to corresponding portions of the other Asserted Patents. All emphases in this brief added unless otherwise noted.

[3] The word "brachytherapy" derives from the Greek word "brachys," which means "short," referring to a short distance. *See* Taber (Ex. 1) at 282.

implantation site will be reduced." *Id.* at 4:21-25. The Summary makes clear that all embodiments of the alleged invention share this advantage.

The rest of the specification further confirms that the patented inventions are directed entirely to targeted, localized delivery of agents to treat or prevent disease. Every single alleged embodiment is directed to facilitating, or capitalizing on the advantages of, localized delivery. Not a single embodiment in the intrinsic record of the Asserted Patents is directed to implants delivering agents to remote tissues.

Microspherix's challenge in asserting these patents against Merck's accused Nexplanon® product is that Nexplanon® is a *birth-control* system including an implant that targets *remote*, *healthy* reproductive tissues with a contraceptive hormone. In other words, Nexplanon® is the opposite of what is described and claimed in the Asserted Patents. In fact, it was not until the filing of the present lawsuit that Microspherix or the alleged inventor, Dr. Kaplan, identified any connection between the asserted brachytherapy patents and contraceptives. Despite decades of development in the field of contraceptive implants prior to Dr. Kaplan's patent filings, the specification does not once refer to contraceptives. Nor does the specification suggest that the alleged invention can be used for all manners of drug delivery—on the contrary, it repeatedly denigrates "conventional systemic administration" of drugs to remote tissues as inferior to the implants for localized treatment that it describes and claims. *E.g.*, '402 Patent at 5:27-45.

As a result, Microspherix proposes claim constructions seeking to expand the asserted claims to cover what the patents expressly distinguish and disparage. Microspherix's constructions are irreconcilable with the claim language, the plain disclosure of the specifications, and the rest of the intrinsic record. Microspherix worsened this problem during the IPR proceedings by successfully arguing that additional, silent claim limitations should save its remaining patent claims. This over-extension drives Microspherix's claim construction positions, and the Court should adopt Merck's proposed constructions—which are consistent with and compelled by the intrinsic record—to prevent Microspherix's improper expansion.

II. FACTUAL BACKGROUND

A. State of the Art in November 2000

The Asserted Patents purport to address the challenge of delivering therapeutic agents to treat localized cancers, where it can be difficult to deliver those agents to tissues that lack sufficient vascular supply (*e.g.* certain tumors) or sit behind the blood-brain barrier (*e.g.* brain cancer). '402 Patent at 5:33-39; Park Decl. ¶¶ 31-33.[4] In such tissues, drug administered systemically (*e.g.* intravenously) may not reach the diseased tissue through the bloodstream in an amount sufficient to treat the disease. Park Decl.¶ 33. Furthermore, it can be difficult or impossible with

[4] The patents are limited not only to localized therapy, but also specifically to localized ***cancer*** therapy. The Court need not reach that issue to accept Merck's positions on the disputed claim construction terms.

systemic administration to achieve a therapeutic concentration of a drug in the diseased tissue without accumulating toxic levels in healthy tissues throughout the body. '402 Patent at 16:59-64; Park Decl. ¶ 54.

To address these concerns when employing radiation therapy to treat cancer, particularly prostate cancer, oncologists use a technique called "brachytherapy," in which physicians carefully space small, radioactive metal seeds within the cancerous tissue to irradiate and kill cancer cells while avoiding exposing remote healthy tissues to the harmful radiation. '402 Patent at 1:30-41. Physicians implant such seeds with precision using image-guided needles to ensure that the radioactive seeds are positioned to provide a safe but effective dose of radiation throughout the volume of the cancerous tissue. Prior art brachytherapy devices employed "spacers" between the seeds to ensure that seeds would maintain their position and orientation within the cancerous tissue to prevent subsequent movement or migration from disturbing the "dosimetry"—the dose of radiation absorbed by the target tissue. *Id.* at 3:9-12, 19:45-46, 22:14-23; *see* Grimm (Ex. 2) at 4:15-17, Fig. 2C.

B. The Alleged Invention of the Asserted Patents

In November 2000, Dr. Kaplan, the applicant, filed a provisional patent application that, following a series of continuations and a continuations-in-part, led to the issuance of the Asserted Patents. The '128 Provisional to which the Asserted

Patents claim priority[5] states that "the invention relates to implantable ***brachytherapy*** devices" and describes implants similar to those it identifies as "conventional radioactive brachytherapy seeds" but that may be made of biodegradable materials (*e.g.* polymers) and may contain a "drug . . . in addition to, or as an alternative to, a radioisotope." '128 Prov. (Ex. 3) at 1, 4. The provisional states that the seeds of the invention "ha[ve] a size and shape suitable for passing through the bore of a ***brachytherapy*** implantation needle" of "any size compatible with ***brachytherapy*** methods." The '128 Provisional does not describe a seed longer than 10 mm, but discloses that seeds "may be conjoined into a chain [] using a plurality of spacers" to "minimize the bunching or straying of seeds [] to avoid over- or under-***dosing of the target tissue*** by the therapeutically active component [] and/or radioisotope," a technique already employed in prior art brachytherapy applications. *Id.* at 29. The '128 Provisional does not disclose contraceptives or any implants designed to target remote tissues.

In September 2002, the applicant filed a second provisional application—the '050 Provisional—primarily adding disclosure related to additional shapes and features of the previously described seeds "to prevent migration or shifting after implantation." '050 Prov. (Ex. 4) at 33, Figs. 3D, 3G). There is no disclosure in the '050 Provisional of contraceptives or any implants designed to target remote tissues.

[5] Merck reserves the right to challenge this priority claim.

In September 2003, the applicant first filed a utility application with the specification substantially as it now appears in the Asserted Patents. This filing includes additional new disclosure but still only addresses localized disease treatment. *E.g.*, '402 Patent at 7:12-61, 9:30-67, 10:1-19, Figs. 8-9; Park ¶ 72. After several continuation applications over fourteen years, and without the disclosure of additional material in the specification, the Asserted Patents issued between 2014 and 2017. Each is titled "Flexible And/Or Elastic ***Brachytherapy*** Seed Or Strand." The entire patent family (those family members asserted in this lawsuit as well as all related patents), is silent as to contraception and silent as to the use of implants to treat diseased tissue ***remote*** to the site of implantation.

C. Merck's Nexplanon® Product

Before the applicant ever filed his earliest provisional patent application, Merck began developing the product at issue in this case, the Nexplanon® system, which launched commercially in 2011, and includes a contraceptive implant that is inserted under the skin of the upper arm to prevent pregnancy for up to 3 years. This implant is not a targeted delivery device, nor does it treat any disease; it provides a contraceptive hormone into the bloodstream to act on remote tissues to prevent pregnancy, just like the several subdermal contraceptive implants that preceded it.

D. The IPR Proceedings

Merck filed and the PTAB granted a petition for IPR for each of the four patents originally asserted in this lawsuit. Microspherix requested adverse judgment and cancelled all challenged claims of the '193 Patent. The PTAB issued three final written decisions on the remaining Asserted Patents, invalidating all challenged claims not limited to implants with some form of "opening." Each surviving claim requires such an opening. *E.g.*, '402 Patent at cl. 9 ("wherein the rod has open ends"). The open-implant claims survived IPR on the sole basis of toxicity concerns raised by Microspherix. Specifically, Microspherix argued, and the PTAB accepted, that a POSA would not have a reasonable expectation of achieving ***what is claimed*** when adding a barium sulfate marker for improved x-ray visibility because ***barium sulfate***, which could leach from the openings, ***is too toxic***. '402 FWD (Ex. 5) at 32[6]. Thus, as a matter of law, Microspherix and the PTAB have already construed the remaining asserted claims (which all have openings) as limited to markers less toxic than barium sulfate. *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016).

[6] Citations to IPR2018-00393 also refer to the corresponding IPR records in IPR2018-00402 and IPR2018-00602, including for example here, '401 FWD (Ex. 30) at 25 and '835 FWD (Ex. 31) at 41.

III. LEGAL STANDARDS

Claims are "generally given their ordinary and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005). The claims are "part of a fully integrated written instrument," and "the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Id.* at 1313, 1315. "Claims must be interpreted with an eye toward giving effect to all terms in the claim," *Becton, Dickinson & Co. v. Tyco Healthcare Grp., LP*, 616 F.3d 1249, 1257 (Fed. Cir. 2010), and "[a] claim construction that gives meaning to all the terms of the claim is preferred over one that does not do so." *Merck & Co. v. Teva Pharm. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005).

"Where the specification makes clear that the invention does not include a particular feature, that feature is deemed to be outside the reach of the claims of the patent, even though the language of the claims, read without reference to the specification, might be considered broad enough to encompass the feature in question." *SciMed Life Sys. v. Adv. Cardiovascular Sys.*, 242 F.3d 1337, 1341 (Fed. Cir. 2001). Such "disclaimer does not require express statements by the patentee identifying the surrendered claim scope" but rather "may be implicit, so long as it is

sufficiently clear." *Rembrandt Patent Innovations, LLC v. Apple, Inc.*, 716 F. App'x 965, 972 (Fed. Cir. 2017). A patentee's statements to the PTO may likewise disclaim subject matter and must be considered during construction, including statements made during IPR. *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576 (1995); *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1360 (Fed. Cir. 2017).

A. Person of Ordinary Skill in the Art

A POSA at the time of the alleged invention would have at least a Master's degree in biomedical engineering, chemical engineering, or a related field with several years of experience with biomedical implants and drug delivery systems. The PTAB accepted this definition during IPR. '402 FWD (Ex. 5) at 4-5.

IV. TERMS RELATING TO LOCALIZED TREATMENT OF DISEASE

A. "target tissue"

"Target tissue" has the meaning that common sense would dictate—it is the tissue *targeted* by the claimed implants. The parties agree that the term refers to at least the location of the implants, but Microspherix ignores that the implants of the Asserted Patents are always located in the tissue they are intended to treat.

Beginning with the language of the claims, Microspherix's proposed construction, *i.e.*, "tissue into which implant is implanted," renders the word "target" meaningless and is therefore improper. *See Teva*, 395 F.3d at 1372 ("A claim construction that gives meaning to all the terms of the claim is preferred over one

that does not do so."); *Becton*, 616 F.3d at 1257. Incorporating Microspherix's proposed construction produces the following tautological claim limitations:

- "the position of the [elongated implant] within a **tissue into which implant is implanted**";
- "upon implantation into a **tissue into which implant is implanted**";
- the "[elongated implant] is configured to be implanted into a **tissue into which implant is implanted** in the subject"

'401 Patent at cls. 1, 6, 19; '835 Patent at cls. 1, 5. Implants are always "position[ed]," "configured to be implanted", and "implante[d]" in the tissue in which they are in fact implanted. Under Microspherix's proposal, the limitation has the same scope as "tissue" alone. *See Componex Corp. v. Elecs. for Imaging, Inc.*, 2014 WL 3556064, at *4 (W.D. Wis. July 18, 2014) ("If [the claim term] was truly meant to have no meaning, the patentee could have deleted [it] from the claims altogether.").

The intrinsic record makes clear that the "target tissue" is where the agent is intended to produce an effect. *Phillips*, 415 F.3d at 1314 (The "proper definition is the definition that one of ordinary skill in the art could ascertain from the intrinsic evidence in the record." (quotation omitted)). The specification consistently focuses on delivery of the therapeutic agent to the "target tissue," and never anywhere else. *See, e.g.*, '402 Patent 17:42-46 ("delivering ***the therapeutically active component*** 14 into a target tissue"); *id*. at 15:42-49, 16:15-24; Park Decl. ¶ 75. The specification claims that an "advantage" of the invention is that it "can provide higher and more

consistent concentrations of a therapeutically active substance ***to a target tissue***." '402 Patent at 5:28-33. The specification addresses the agent reaching other tissues only when discussing potential *negative side effects*, not any intended benefit. *Id.* at 4:21-25 ("any potential ***deleterious effect*** of the therapeutically active substance on ***healthy tissue located away from the implantation site*** will be reduced").

The specification focuses on the delivery of the therapeutic agent to the "target tissue" because it is the "target tissue" that requires treatment. The "Methods of Implantation" section notes that "***to treat a given target tissue*** with a therapeutic agent" it is "[i]n many applications" "desirable (or even ideal) to ***fully saturate the target tissue*** with the therapeutic agent." *Id.* at 23:41-44. When describing the utility of the claimed "marker," the specification even expressly states that "***the site of the disease***" to which "the therapeutically active component [] is delivered" is "***in the target tissue***." *Id.* at 18:21-25. The earliest provisional through the Asserted Patents all describe the advantage of structures and methods that assist with "***dosing of the target tissue***" by ensuring that the implants are precisely spaced and positioned therein. '128 Prov. (Ex. 3) at 29 (disclosing "spacers" employed "to avoid over- or under-dosing of the target tissue by the therapeutically active component [] and/or radioisotope."); '402 Patent at 23:41-44 (precise implantation techniques to "avoid[] under- over-dosing the target tissue").

The specification even employs the term "target tissue" when referring to the tissue targeted by an agent that was introduced into the bloodstream, including by oral or intravenous delivery (*i.e.* with no implant at all). '402 Patent at 5:28-39 ("brachytherapy strands" of the invention can "circumvent ***delivery problems*** such as where ***a target tissue*** lacks an intact vascular supply (e.g., ***a target tissue*** whose ***blood flow may be compromised***) or is otherwise ***sequestered from the blood supply***"). Therefore, the hallmark of a "target tissue" is that it is the tissue on which the agent acts to produce its intended effect. In the context of the claimed invention, in which the brachytherapy implants are implanted into the tissue they target, the "target tissue" is *also* the tissue into which implantation is intended.

The specification uses other terms when referring solely to the location of the implant in the subject. Park Decl. ¶ 78. In one instance, the patent distinguishes the "target tissue" to which "all or part of the therapeutically active component will be delivered" from the "implantation site" into which "the brachytherapy strand 10 is introduced." '402 Patent at 15:42-49. The patent also distinguishes a "target tissue" from "the environment surrounding the strand," which may include tissue that is not "targeted." '402 Patent at 16:18-24; *id.* at 19:41-45 (describing the "logistical problems" presented by "irregularly shaped targets" or "targets that are split by intervening tissue that one wishes to avoid").

Moreover, a POSA reading the specification would recognize that every embodiment of the invention is directed to treating disease in tissues local to the site of implantation.[7] Park Decl. ¶ 79. Since the first provisional application, the inventor has consistently described the alleged invention using the term "brachytherapy," which necessarily refers to localized treatment. *Id.* The Summary describes the advantage of the implants of the invention in the same manner the patent describes the advantage of conventional brachytherapy:

> Since concentrations of the therapeutically active substance will be greater at the implantation site (e.g., the diseased tissue), any potential deleterious effect of the therapeutically active substance on healthy tissue located away from the implantation site will be reduced.

Compare '402 Patent at 4:21-25, *with id.* at 1:36-39 (describing an identical advantage for prior-art brachytherapy "[b]ecause the seeds are ***localized near the diseased tissue***"). This localized delivery in the target tissue allows for the use of "a drug that is usually considered too toxic to treat a given condition if given systemically," such as certain chemotherapeutics. '402 Patent at 16:59-64. Other disclosed aspects of the invention are expressly designed to assist with such localized treatment, including the claimed marker and anchoring/spacing structures, which

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[7] The specification's listing of prior-art publications regarding the association of therapeutic agents with biocompatible components at columns 8-9 of the specification does not purport to describe potential embodiments of the invention, but rather demonstrates the state of the art, including even outside the context of human administration. Park Decl. ¶ 42 (noting that one such publication, for example, describes laboratory application for separating cells in vitro).

ensure precise control over the delivery of agents to tissues local to the site of implantation. Park Decl. ¶ 79. The intrinsic record never suggests that the implant may be located remotely to the tissue on which the agent is intended to act and in fact expressly distinguishes such systemic delivery as inferior. *Id.* ¶ 80. Thus, the tissue on which the agent acts to produce its intended effect and the tissue in which the implantation is intended must be one and the same.

The intrinsic record's use of "target tissue" is consistent with the common use in the art of the term "target" to describe the focus of the treatment (*e.g.* "targeted drug delivery"). *Id.* ¶ 81. While the term "target" automatically evokes the intended site of action for the drug, it is the brachytherapy context and the express disclosure of localized treatment that tells a POSA that the "target tissue" is *also* the tissue in which implantation is intended. *Id.* Microspherix's construction as "tissue in which [the] implant is implanted," ignores the *most common* association of the term—the target of the intended treatment.

In overreaching to encompass Merck's Nexplanon® product, Microspherix attempts to redefine "target tissue" in a manner inconsistent with both the intrinsic record and common usage. The Court should adopt Merck's construction.

B. "seed, for implantation into a subject" / "strand for administration of a therapeutic agent to a subject in need thereof" / "strand for implantation into a subject"

As described above, the specification is explicit that the sole use of the

disclosed implants is for the localized treatment of disease, and that for the implants to have their intended effect, they must be implanted at the site where the agent produces its intended effect. "Where the specification makes clear that the invention does not include a particular feature, that feature is deemed to be outside the reach of the claims of the patent, even though the language of the claims, read without reference to the specification, might be considered broad enough to encompass the feature in question." *SciMed*, 242 F.3d at 1341; *see also Watts v. XL Sys., Inc.*, 232 F.3d 877, 882 (Fed. Cir. 2000); *Wang Labs., Inc. v. America Online, Inc.*, 197 F.3d 1377, 1383 (Fed. Cir. 1999). Requiring that seed/strand be implanted near the site on which the agent acts to produce its intended effect (and vice versa) is compelled by the applicant's express and uniform description of his invention and is consistent with Microspherix's position that the preambles are limiting. *See* MX Ev. (Ex. 6) at 4.

In his first provisional filing, the applicant set forth his invention as "relat[ing] to implantable brachytherapy devices." '128 Prov. (Ex. 3) at 1. The Asserted Patents disclose the "Background of the Invention" as "brachytherapy," which they set forth as the use of radioactive seeds to treat cancer by spacing them carefully within the cancerous tissue. '402 Patent at 1:30-2:16. While the alleged invention may have expanded brachytherapy to employ drugs in addition to/in place of radiation, *see id.* at 3:67-4:3, Microspherix now attempts to stretch "brachytherapy"

beyond the *localized* treatment of disease, rendering the titular adjective describing every embodiment of the Asserted Patents meaningless and ignoring the very root of the word "brachytherapy." *See supra* note 4. In prosecution of a related patent stemming from the same provisional application to which Microspherix claims priority, the applicant personally represented to the PTAB that his invention addresses the need for an implant that provides localized saturation of drugs in diseased tissues:

> There is no such thing as image guided saturation of a tumor with a drug today. It doesn't exist. This is an excellent attempt, I believe, to fill a void that is sorely needed, at least in the cancer population. *There is no way to saturate a tumor peripherally when you give chemotherapy by vein*. The chemo goes all throughout the body. *There is no way to inject the tumor where distribution of the drug is even and can be measured*.

1/12/12 Pros. Tr. (Ex. 7) at 11:9-17. Consistently, there is not a single disclosure in the intrinsic record indicating that the applicant expanded "brachytherapy" beyond localized treatment.

The two short paragraphs of the Summary expressly demonstrate that the invention is limited to localized treatment of disease. As in the Title and Abstract, the first sentence of the Summary establishes the implants of the invention as "brachytherapy" implants, consistent with the remainder of the specification. '402 Patent at 3:66. This is an express limitation of the implants of the invention to localized treatment that must inform claim construction. *SciMed*, 242 F.3d at 1341. The remaining summary likewise presumes the invention is limited to localized

therapy, stating that "concentrations of the therapeutically active substance ***will be greater*** at the implantation site" and thus "any potential deleterious effect of the therapeutically active substance on healthy tissue located away from the implantation site ***will be*** reduced." '402 Patent at 4:21-25. This statement is inconsistent with implants in which the tissue targeted by the therapeutic agent is remote to the site of implantation, and in fact distinguishes systemic drug administration as inferior. *Id.* at 4:21-25, 5:28-33, 16:59-64. These disclosures show that Dr. Kaplan is describing all embodiments as employing targeted, localized treatment, requiring Merck's constructions. *SciMed*, 242 F.3d at 1344; *see also Rembrandt*, 716 F. App'x at 972 ("[D]isclaimer does not require express statements by the patentee identifying the surrendered claim scope. Rather, it may be implicit, so long as it is sufficiently clear."). The Examiners who reviewed the applications leading to Asserted Patents (including those applications in their chain of priority) apparently recognized this limitation, consistently restricting their prior-art searches to classifications related to radioactive therapy and/or "brachytherapy." *See, e.g.*, '401 FH Srch. (Ex. 32) (searching A61K51/00, the Cooperative Patent Classification for "Preparations containing radioactive substances for use in therapy or testing in vivo," available at https://www.uspto.gov/web/patents/classification/cpc/html/cpc-A61K.html#A61K51/00).

These general statements are particularly strong indications that Dr. Kaplan intended to limit all embodiments of his invention. *See C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 864 (Fed. Cir. 2004) ("Statements that describe the invention as a whole are more likely to be found in certain sections of the specification, such as the Summary of the Invention," and "other things being equal, [such] sections of the specification are more likely to contain statements that support a limiting definition of a claim term than other sections[.]"); *Wireless Protocol Innovations, Inc. v. TCT Mobile, Inc.*, 771 F. App'x 1012, 1018 (Fed. Cir. 2019) ("The repetition of that language in sections meant to describe the overall invention, together with the uniformity of the specification on this point, makes clear that [the feature] is not merely a preferred embodiment for the [claim term], but rather a requirement."); *Virnetx, Inc. v. Cisco Sys., Inc.*, 767 F.3d 1308, 1318 (Fed. Cir. 2014) ("The fact that the Summary of the Invention gives primacy to [both security and anonymity] strongly indicates that the invention requires more than just data security.").

Furthermore, every feature of the disclosed brachytherapy implants are uniformly directed to improving their use in the context of localized treatment. The specification describes anchoring structures to prevent implant migration and maintain orientation to preserve dosimetry—the pattern of radiation absorption immediately surrounding a radioactive implant. Park Decl. ¶ 60; '402 Patent at

19:22-20:13, 31:16-22:7. The patent's express purpose for including a "marker" in the invention is to assist precise placement within a diseased tissue. '402 Patent at 18:21-25, Park Decl. ¶¶ 57-58. The implants are designed for use with pre-existing brachytherapy implantation devices that carefully space implants within the diseased tissue. '402 Patent at 23:31-34, 41-58; Park Decl. ¶¶ 63-64.

The specification is silent as to any alternative to placing the implant locally to the diseased tissue. *See Virnetx*, 767 F.3d at 1318 ("The fact that anonymity is repeatedly and consistently used to characterize the invention strongly suggests that it should be read as part of the claim," despite "mechanical[]" use of prefacing phrases "it may be desired" or "according to one aspect of the present invention," where patentee "has not identified even a single embodiment that provides data security but not anonymity."); *Toro Co. v. White Consolidated Industries, Inc.*, 199 F.3d 1295, 1301 (Fed. Cir. 1999) (limiting the claims where "[n]o other, broader concept was described as embodying the applicant's invention, or shown in any of the drawings, or presented for examination"). For example, despite decades of research and publications regarding systemic, contraceptive, polymeric implants, Dr. Kaplan does not once refer to this art despite citing hundreds of prior art patents and publications in the specification. Park Decl. ¶ 86. Nor does the specification address the distribution of drug in the bloodstream, except to distinguish systemic

delivery as inferior. *Id.* ¶¶ 27-28. The patent should not be read to have a scope it does not describe or enable. *Wang*, 197 F.3d at 1383.

As in *SciMed*, the specification's repeated limitation of the invention to "brachytherapy," an indisputably localized form of therapy, requires a limiting construction. *See* 242 F.3d at 1344 (finding it was "difficult to imagine how the patents could have been clearer in making the point that coaxial lumen configuration was a necessary element of every variant of the claimed invention" when describing it as "the basic [] structure for all embodiments of the present invention"). In *Rembrandt*, the Federal Circuit found that the claims in a patent directed to initializing a computer system were limited to ***automatic*** recovery where the specification set forth the advantage of automation in the Summary of the Invention ("the total cost of ownership is reduced 'through **automatically** detecting and repairing integrity failures'"), and where the specification lacked embodiments without automatic recovery and expressly "criticiz[ed] . . . prior art recovery methods that involved human intervention." 716 F. App'x at 971-72 (emphasis in original). This is precisely how Dr. Kaplan has treated localized delivery: touting it as an advantage of the invention, failing to disclose alternative embodiments, and distinguishing non-localized, systemic administration as inferior. The Court should limit the claims in accordance with Dr. Kaplan's express limitation of his own alleged invention.

C. "therapeutic agent" / "prophylactic agent"

The terms "therapeutic" and "prophylactic" have commonly accepted definitions that the specification of the Asserted Patents only reinforces. POSAs reading the patent would recognize these terms-of-art and know that "therapeutic agents" are agents for the treatment of disease and "prophylactic agents" for the prevention of disease. Park Decl. ¶ 83; *Phillips*, 415 F.3d at 1313 ("[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art[.]"). These commonly accepted definitions are uniformly reflected in medical and English-language dictionaries at the time of the invention. *See* Stedman (Ex. 8) at 1458, 1821; Taber (Ex. 1) at 1763, 2170; Merriam (Ex. 9) at 670, 824; Mosby (Ex. 10) at 1413.

The specification not only uses these terms consistently with their commonly accepted meanings, but also reinforces that the agents relate to the treatment and prevention of disease. As discussed above, the "Abstract," "Background of the Invention," and "Summary of the Invention" disclose that the invention is one in the field of "brachytherapy," which is the localized treatment of cancer. The "Detailed Description of the Invention" is organized by sections, the first being titled "I. Brachytherapy Strands," under which the subsection titled "C. Therapeutic and Diagnostic Agents" falls. '402 Patent at 5:46, 7:62. It is thus under the umbrella of "brachytherapy" that the "therapeutic agents" are disclosed.

Subsection I.C. states that "any of a wide range of ***therapeutic***, diagnostic[8] and ***prophylactic*** materials can be incorporated into the strands," '402 Patent at 7:67-8:3. The adjectives "therapeutic" and "prophylactic" bound the disclosure of active agents in the patent. Every exemplary drug in the patent is for the treatment or prevention of disease. Park ¶¶ 41-42, 85. Each background prior art publication in this section also concerns the treatment or prevention of disease. *Id.*

Consistent with the specification's focus on disease, the patent does not once refer to contraceptive agents, which are not "therapeutic" or "prophylactic." Contraceptives prevent pregnancy, which is not a disease. *Id.* ¶ 86. Skilled artisans have expressly distinguished between therapeutic and contraceptive agents in the prior art. *Id.*; Fraser (Ex. 11) at 990 (noting that the "agonists may have therapeutic ***as well as*** contraceptive actions in women[.]"). The applicant does not cite a single reference regarding contraceptive agents despite numerous prior art publications regarding the decades of clinical and commercial use of contraceptives "associated with biocompatible materials for use in drug delivery systems." '402 Patent at 8:16-18; Park Decl. ¶ 86. This absence of contraceptive agents in the disclosure confirms that the applicant did not expand the definition of "therapeutic agent" or "prophylactic agent" beyond their ordinary association with disease. *Straight Path IP Grp., Inc. v. Sipnet EU S.R.O.*, 806 F.3d 1356, 1361 (Fed. Cir. 2015) ("When

[8] "Diagnostic' is not a term in dispute here.

claim language has as plain a meaning on an issue as the language does here . . . it is particularly difficult to conclude that the specification reasonably supports a different meaning." (quoting *Phillips*, 415 F.3d at 1316, 1323, 1324)).

The Court should credit the intrinsic record, the stated field of the invention (brachytherapy), the common understanding of the terms, and the express disclosure of the specifications, and adopt Merck's proposed constructions.

V. TERMS RELATED TO CONFIGURATION OF THE IMPLANTS

A. "marker component"

Consistent with the use of the term "component" in the specification and claims, the "marker ***component***" is ***the*** part of the seed or strand that ***is a marker***. In the claims, the term "component" refers to distinct aspects of the implants—the "marker component" and the "biocompatible component." The specification never uses the term "marker component" outside of the claims, but it uses the terms "biocompatible component," "therapeutically active component," and "biodegradable component." Each term refers to the part of the implant that has its respective characteristic (*i.e.* the part that is biocompatible, therapeutically active, or biodegradable). By using the term "component" within its proposed construction, Microspherix provides no actual construction for the term "component." The Court should adopt Merck's construction as consistent with the intrinsic record and to avoid the ambiguity of Microspherix's construction.

B. "hollow interior" / "wherein the agent is disposed within the hollow interior of the tube"

Merck proposes that the term "hollow interior" be construed in a common-sense manner that gives meaning to the term "hollow." Merck's proposal is consistent with both the language of the specification and the commonly understood meaning of the term. In contrast, Microspherix's proposed construction —"interior space"—nullifies entirely the word "hollow" from the claim limitation, and therefore cannot be correct. *See Teva*, 395 F.3d at 1372; *Becton*, 616 F.3d at 1257.

The claims themselves demonstrate that "hollow interior" has the plain meaning that Merck proposes. They describe the hollow interior as a structure with a "diameter" that is configured to have other components "disposed within" it, including an agent that may "pass out" through "at least one opening." This comports with a structure having an "empty space," leaving room for other components to fill and subsequently vacate the interior. In the context of the claim language, the "hollow interior" is specifically the empty space defined by and inside the wall of the marker component, which "***bounds***" it. *E.g.*, '835 Patent cl. 1 ("marker component . . . having a substantially continuous wall ***bounding*** a hollow interior"). The same is true in the context of '835 Patent claim 20, where "the agent is disposed within the hollow interior ***of the tube***," which is itself the structure of the "marker component . . . having a substantially continuous wall." '835 Patent cl. 20. The claims thus dictate Merck's construction.

The specification likewise supports Merck's construction. It does not use the term "hollow interior," but does use the term "hollow" in two instances: it describes Fig. 2 as "a hollow tube-shaped brachytherapy strand," which it describes as "having a cylindrical ***cavity***" and a "wall thickness" suitable for encompassing other strands. '402 Patent at 4:31-32, 15:22-41. The specification also refers to "hollow viscera" "such as the urinary bladder," where "loose seeds cannot be reliably spaced out owing to ***a dearth of tissue*** and the associated risk of losing the seeds into the ***lumen or cavity*** of the organ." '402 Patent at 2:59-66, 3:9-12. The specification thereby demonstrates that the term "hollow" denotes an empty space, consistent with its common definition as "having a cavity or space inside" (Taber (Ex. 1) at 997) or "having a cavity, hole, or space within" (Webster (Ex. 12) at 528).

Microspherix's proposed construction, *i.e.*, "interior space," renders the term "hollow" meaningless, and is indistinct from simply "an interior." An "interior space" could be hollow or not hollow. The claim's use of the term to modify "interior" has meaning, and Microspherix's proposed construction must therefore be rejected. *See Teva*, 395 F.3d at 1372; *Becton*, 616 F.3d at 1257.

C. "[marker component] . . . having a substantially continuous wall bounding a hollow interior" / "[marker component] . . . having a substantially continuous wall along the length, the substantially continuous wall bounding a hollow interior"

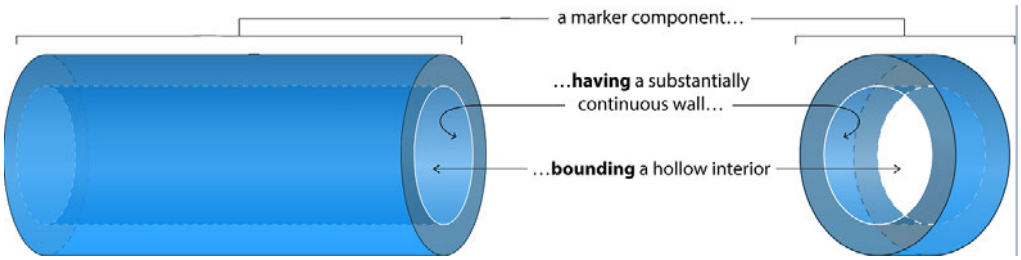
Merck's construction is dictated by the plain language of the claims themselves. The claims describe a "marker component" as "***having*** a substantially

continuous wall ***bounding*** a hollow interior." The word "having" connotes that a part of the marker component itself (*i.e.* the "wall") "bound[s]' and therefore defines the hollow interior. Claim 20 of the '835 Patent provides an example configuration in which the marker component also "compris[es] a tube having open ends." Because the marker component "***has***" a wall and "***comprises*** a tube," the marker component must itself constitute the structure bounding the hollow interior. This is consistent with the specification's description of Fig. 2 as a "hollow tube" that "has" a "wall." '402 Patent at 15:36-41. Every instance of the word "having," "have," or "has" in the specification refers to a physical feature of the object being described. *E.g.*, *id.* at 16:20-21 ("cylinder ***having*** a plurality of pores through its outer surface").

Microspherix proposes a construction that merely imports its definition of "marker component" and fails to meaningfully construe the remaining claim language. This failure is explained by Microspherix's infringement contentions, where Microspherix asserts the barium sulfate ***in the solid, rod-shaped core*** of Merck's Nexplanon® implant is the "marker component," but fails to explain how ***Nexplanon®'s barium sulfate itself*** "has" a substantially continuous wall or "bound[s]" a hollow interior. *See, e.g.*, MX Inf. Cont. (Ex. 13) at 24-25 ('401 Patent cl. 1: "Barium sulfate is therefore a marker component in Nexplanon.").

Looking at the configuration of the claimed implants also confirms Merck's proposed construction. The '835 and '401 Patent claims recite a structure with two

regions: 1) the "marker component," which "has a substantially continuous wall" and "bound[s] a hollow interior," and 2) the "hollow interior" in which other components are disposed (*e.g.* the "therapeutic, prophylactic, and/or diagnostic agent"). The "marker component" is thus illustrated by the below, exemplary diagram:



Merck's proposed construction, where the marker component "itself constitutes a wall that defines a hollow interior," is the only logical interpretation of the claim language.[9] The Court should therefore adopt Merck's construction.

[9] Some claims of the '401 and '835 Patents have additional limitations that present facial ambiguity due to lack of antecedent basis. For example, '401 Patent claim 1 has a limitation requiring that "***the*** marker" be "disposed within the hollow interior," but provides no antecedent basis for "marker," only a "marker component," which logically cannot be disposed within its own interior. The rest of the claim language and the intrinsic record resolve this ambiguity by making clear that "the marker" must be interpreted as "***a*** marker" (solving the antecedent problem), such that the claim contemplates, in addition to the "marker component," additional "marker" disposed within the hollow interior that can pass out of the interior and into the patient's body. Specifically, claim 1 recites "a therapeutic, prophylactic, and/or diagnostic agent … disposed within the hollow interior" and that "the substantially continuous wall includes at least one opening adapted to allow ***the agent*** to pass out of the hollow interior." The specification in turn uses "diagnostic agent" as an umbrella term encompassing markers (*see* '402 Patent at 5:18-19, 10:20-22). Thus, the claim covers an implant that has a "marker" that can pass out of the hollow interior of the "marker component." As the applicant explained to the Patent Office

D. "polymeric coating"

A "polymeric coating" is a common feature of biomedical implants, and skilled artisans use the term to refer to layers of polymer that are applied to existing surfaces, often to protect the devices or to form a membrane that controls the rate of drug release. Park Decl. ¶¶ 88-89. The language of the claims does not suggest that the term has a special definition within the context of the '402 Patent, and the specification confirms that "coating" has its customary meaning. Microspherix's construction of "polymeric coating" as "a layer of polymer" is improper for several reasons, including that it reads out the word "coating," is inconsistent with the intrinsic record of the Asserted Patents, and conflicts with Microspherix's own usage of the term.

The specification of the Asserted Patents does not use the term "polymeric coating" but does employ the term "coating" in reference to polymers. The specification uses "coating" while describing one of the most common prior art coating processes which uses a "Fluidized Bed." In the fluidized bed process, existing "particles," "seeds," or "strands" are suspended in "a vertical column of heated air" while "an atomizing nozzle . . . ***applies the coating material*** in the form of a [liquid] spray." '402 Patent at 13:36-14:19. The "coating fluid," such as the

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during prosecution of a related patent, releasing a marker with the agent "allows you to sort of shadow or map the distribution of the drug throughout the site of treatment, such as a tumor." 1/12/12 Pros. Tr. at 3:9-13.

polymer "polyethylene glycol," "is readily ***distributed onto the surface of the seeds or strands*** in the moving bed" and thus "a uniform coating is ***built up on the seeds or strands***." *Id.* This comports with the common definition of "coating," referring to a layer that is "coated" on an existing surface. *See also id.* at 21:11-12 ("the strand ***is coated*** with a non-radioactive biodegradable ***coating***").

Microspherix itself has repeatedly admitted that a coating is not a generic "layer of polymer": by drawing distinctions between various types of layers of polymer in the intrinsic record and in this litigation. Claims in the same Microspherix patent family distinguish between a "coating" and a "sleeve." '310 Patent (Ex. 14) at cls. 39-42 ("structures are in the form of a ***coating or sleeve***"). The specification distinguishes between polymers used "to form" implants and polymers used "to coat" implants. *Id.* at 7:63-64 ("Polymers can be used to form, ***or*** to coat, drug delivery devices such as strands[.]"); *see also id.* at 13:37-38. The specification does not once use the term "coating" to refer to a layer that was not applied to an existing surface. For example, the specification does not refer to the housing of a tube or capsule as a coating, even where those structures are "layer[s] of polymer" filled with other substances and thus surround them. *See id.* at 17:16-59, Fig. 2. [redacted]

[redacted]

Microspherix's repeated distinction between certain layers of polymers surrounding a structure, such as a hull or sheath or sleeve, and a "polymeric coating" reveals the fatal flaw in their own proposed construction: it reads out the meaning of "coating" entirely. Under Microspherix's construction, the term could be reduced from "polymeric coating" to "polymer" without changing the claim scope (*i.e.* "a [polymer] . . . wherein the [polymer] covers the strand"). This further indicates that Microspherix's proposal should be rejected. *See Teva*, 395 F.3d at 1372; *Becton*, 616 F.3d at 1257.

Microspherix's proposed construction is once again driven by its infringement positions against Merck's Nexplanon® product, which has no "coating." [redacted]

[redacted] The Court should reject Microspherix's litigation-driven and improper proposed construction.

E. "rod"

The parties appear to agree that a rod is cylindrical but dispute whether the term means "a unitary cylinder" or a "cylinder-shaped device." Merck's construction makes clear that the claimed rod is one unit, which is necessary in light of the claimed configurations of strand (of which "rod" is a sub-species).

The specification discloses strands formed as chains or continuous arrays of seeds (including cylindrical seeds) that are connected by a plurality of spacers. '402 Patent at 4:9-12. While a chain of cylindrical seeds could generally be cylinder *shaped*, a chain of seeds cannot be a "rod" because it is not unitary. Figs. 5A and 5B from the '128 Provisional (shown below) are illustrative.

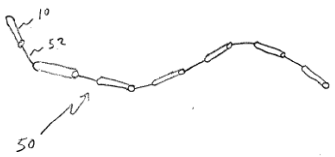

FIG. 5A

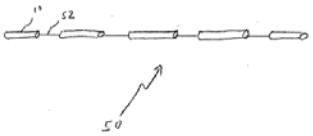

FIG. 5B

Rather, a rod is a single, unitary structure as illustrated in Figs. 1 and 2 of '402 Patent. Merck's construction takes into account the single "rod" in the specification and distinguishes it from the "chain of seeds." *See Medicines Co. v. Mylan, Inc.*, 853 F.3d 1296, 1309 (Fed. Cir. 2017) (recognizing that claim scope can be defined by an

embodiment). Merck's construction is also supported by technical dictionaries. *See* Dorland (Ex. 17) at 1639; Stedman (Ex. 18) at 1577; *see also Vanguard Prods. Corp. v. Parker Hannifin Corp.*, 234 F.3d 1370, 1372 (Fed. Cir. 2000) (affirming construction based on dictionary). The Court should adopt Merck's construction.

F. "flexible"

The intrinsic record does not teach a POSA what degree of flexibility is required by the claims, despite Microspherix's characterizing flexibility as a "primary purpose" of the invention. '401 POR (Ex. 19) at 12. The patent gives no boundary as to what is and is not "flexible," nor provides any special meaning for the term, despite its appearance in the title, abstract, and preamble of every claim. The term is indefinite. Consistent with this Court's practice, Merck will raise its indefiniteness arguments at the merits phase. JCCPS (D.I. 94-1).

To the extent "flexible" is capable of construction at *Markman*, the Court should adopt Merck's proposed construction of "capable of bending." Merck's construction is consistent with the ordinary meaning of "flexible," as supported by Microspherix's own arguments and expert testimony during IPR ('401 POPR (Ex. 20) at 7-8) (Microspherix proposing "flexible" as "capable of being flexed: capable of being turned, bowed, or twisted without breaking."); *see also* Kiser Decl. (Ex. 21) ¶ 66. The specification is not inconsistent. '402 Patent at 2:66-3:8, 3:66-4:11, 5:4-5:9, 19:59-63, 22:23-50, 23:8-12. Departing from its position in the IPR,

Microspherix now advances a construction relying on what flexible *is not* (*i.e.* "not rigid or flaccid"). But the specification reveals that flaccid and rigid are not exclusive of flexible. *See id.* at Abstract, 4:8-11, 22:23-25 ("Where the spacer is made of a relatively flexible material, the chain can be relatively flaccid."), 22:32-35 ("Where the chain is endowed with the flexibility of an elastic polymer or similar substance, the chain may be considered to be variably flexible rather than rigid or flaccid."). The Court should reject Microspherix's construction as unsupported.

VI. CONSTRUCTIONS NECESSITATED BY THE IPR RECORD

A. "marker" / "radiopaque material" / "radio-opaque material" / "agent selected from the group consisting of radiopaque"

Microspherix resisted Merck's obviousness challenge of the asserted claims surviving IPR by successfully convincing the PTAB that ***barium sulfate***, a well-known radiopaque marker used with implants for decades, is too toxic to be a radiopaque marker in the context of claims that require the implants to have open ends, openings, or pores through which a marker could theoretically escape. Microspherix's successful IPR argument hinged on a finding by the PTAB that all surviving claims are limited to having markers less toxic than barium sulfate. That construction should apply equally here.

1. MX successfully argued toxicity is an element of the asserted claims

During IPR, Microspherix argued, and the PTAB accepted, that toxicity is relevant to "marker," "radiopaque material," and "agent . . . selected from the group

consisting of . . . radiopaque." Merck asserted that certain claims of the challenged patents, including all of the Asserted Claims, would have been obvious in light of a combination of two prior art patents, one of which teaches the use of barium sulfate as a radiopaque marker in a contraceptive implant. This combination of references included every limitation in the asserted claims. *See, e.g.*, '402 FWD (Ex. 5) at 27. Where a patent claim is composed of elements found in the prior art, the claim is obvious where there is ***both*** 1) a motivation that would have prompted a POSA to combine the elements in the claimed way, ***and*** 2) "a reasonable expectation of success from doing so." *PAR Pharm., Inc. v. Twi Pharms., Inc.*, 773 F.3d 1186, 1193 (Fed. Cir. 2014).

Microspherix disputed a POSA would have been motivated to combine a barium sulfate marker with open-ended implants. Critically, Microspherix also repeatedly argued that a POSA would not have had a ***reasonable expectation of success*** in achieving an open ended implant with barium sulfate because of its potential toxicity as a marker or radiopaque agent/material. *See, e.g.*, '402 POR (Ex. 22) at 61-62 (arguing that "POSAs ***would not have expected to succeed*** in adding a marker component to an implant with an opening" because of concerns about "adverse effects" from the toxicity of barium sulfate); '402 POSR (Ex. 23) at 14 (arguing that potential adverse effects from barium sulfate leaching "certainly mattered to POSAs—and whether they would be motivated to pursue the

combination ***with an expectation of success***."); IPR Hr'g Tr. (Ex. 24) at 65:24-66:8, 96:23-97:1 (counsel for Microspherix identifying concerns about toxicity of barium sulfate as a reason for a lack of expectation of success).

The PTAB accepted Microspherix's argument that the potential toxicity of barium sulfate defeated a POSA's reasonable expectation of success:

> Because barium sulfate was known to be toxic and leaching of the material from devices was a concern to an ordinary artisan at the time the invention was made, we are not persuaded that Petitioner has shown a person of ordinary skill in the art to have had ***a reasonable expectation of successfully*** combining De Nijs and Schopflin for purposes of claims 6 and 9.

'402 FWD (Ex. 5) at 32. The Federal Circuit upheld the PTAB's decision. *Merck Sharp & Dohme Corp. v. Microspherix LLC*, 814 F. App'x 575 (Fed. Cir. 2020).

The Federal Circuit has made clear that whether a POSA would have a reasonable expectation of success in pursuing an obviousness combination applies ***only to claim elements***—whether express or implied.

> The reasonable expectation of success requirement refers to the likelihood of success in combining references ***to meet the limitations of the claimed invention***. Failure to consider the appropriate scope of the patent's claimed invention in evaluating the reasonable expectation of success constitutes a legal error that is reviewed without deference.

Illumina, 821 F.3d at 1367. Microspherix counsel conceded this at the hearing on the IPRs. IPR Hr'g Tr. (Ex. 24) at 65:24-66:8 (counsel for ***Microspherix agreeing that reasonable expectation of success is "success in achieving what's claimed.***"). Thus, in holding that there would be no expectation of success in using barium

sulfate because of its toxicity, the PTAB necessarily found the level of toxicity to be a claim limitation. Otherwise, toxicity would have no relevance to the determination of a reasonable expectation of success.

Microspherix is well aware that this argument imposed toxicity limits on the claims, and that the PTAB understood this as well. The PTAB cited the *Illumina* decision in rejecting a separate basis presented by Microspherix for a lack of reasonable expectation of success, namely that the inclusion of a radiopaque marker could alter the release rate of the therapeutic agent. The PTAB rejected this argument because it found that the release rate of the therapeutic agent was not claimed subject matter. '402 FWD (Ex. 5) at 25-26 ("Patent Owner's arguments relating to the release rate of the therapeutic agent ***relates to unclaimed subject matter***.") (citing *Illumina*). Rejecting Microspherix's arguments regarding release rate (as unclaimed matter) yet accepting Microspherix's arguments as to toxicity reflects the PTAB's acceptance that toxicity of the radiopaque marker must be (silent) claimed subject matter.[10] These terms should thus be limited to substances "less toxic than barium sulfate."

2. Microspherix's arguments constitute IPR disclaimer

[10] The Court need not at this time determine what level of potential radiopaque marker or material is too toxic. What is clear is that the PTAB and Microspherix drew a bright line that barium sulfate was too toxic within the claims.

Microspherix's position at the PTAB was a disclaimer of toxic markers from the claim scope. Microspherix should not be allowed to introduce a new claim limitation (level of toxicity) in one proceeding in order to establish validity, and then argue broader claim scope when asserting the patent in another proceeding. *See, e.g.*, *Aylus*, 865 F.3d at 1360 (the Federal Circuit "[e]xtending the prosecution disclaimer doctrine to IPR proceedings will ensure that claims are not argued one way in order to maintain their patentability and in a different way against accused infringers."). And as discussed above, Microspherix's argument that a POSA would not have a reasonable expectation of success *necessarily depends* on level of toxicity being a claim limitation, or toxicity would be irrelevant to the reasonable expectation of success. The claim terms at issue should be construed to be at least less toxic than barium sulfate, as the principle of prosecution history disclaimer "limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution." *Southwall*, 54 F.3d at 1576.

3. MX's arguments are highly relevant to claim construction

Even outside of a strict application of prosecution history disclaimer, Microspherix's reasonable expectation of success argument concerning toxicity is strong evidence in favor of Merck's construction, as reasonable expectation of success cannot apply without being tied to a claim limitation. *See, e.g.*, *Illumina*. Positions taken by the patent owner need not qualify as prosecution history

disclaimer to inform the court's claim construction. *See, e.g.*, *Shire Dev., LLC v. Watson Pharm*., *Inc*., 787 F.3d 1359, 1366 (Fed. Cir. 2015) (finding that while "the prosecution history statements do not rise to the level of unmistakable disavowal, they do inform the claim construction"); *MasterMine Software, Inc. v. Microsoft Corp*., 874 F.3d 1307, 1312 (Fed. Cir. 2017); *Personalized Media Commc'ns, LLC v. Apple Inc.*, 952 F.3d 1336, 1346 (Fed. Cir. 2020) (holding statements made by the applicant "decisive as to the meaning of the disputed claim term—even if those statements do not rise to the level of a disclaimer."). Here, reliance by Microspherix and the PTAB on reasonable expectation of success to find lack of obviousness necessarily assumed that level of toxicity is an element of the claims. *See, e.g.*, *Nuvo Pharms. (Ire.) Designated Activity Co. v. Dr. Reddy's Labs. Inc.*, 923 F.3d 1368, 1379 (Fed. Cir. 2019) (analyzing the written description for the term "therapeutically effective amount" after the parties agreed it was a limitation required by the claims).

4. Microspherix's claim constructions are also barred by judicial estoppel

Microspherix is estopped from arguing that toxicity of the marker is not a limitation on claim scope under the principle of judicial estoppel. Judicial estoppel applies when a patent owner makes arguments that are inconsistent with statements successfully made during prior proceedings. *See, e.g.*, *Lampi Corp. v. Am. Power Prod., Inc*., 228 F.3d 1365, 1377 (Fed. Cir. 2000) (applying judicial estoppel to administrative proceedings such as IPR). Judicial estoppel is found where (1) a

party's later position is clearly inconsistent with its earlier position; (2) the party succeeded in persuading a court to accept the earlier position; and (3) the party would derive an unfair advantage over the opposing party. *New Hampshire v. Maine*, 532 U.S. 742, 750–51 (2001) (citations omitted).

First, Microspherix's current position that the "marker" terms do not include any limitation on toxicity conflicts with its IPR position that the toxicity of barium sulfate as a radiopaque marker negates a reasonable expectation of success of making the claimed invention. *See, e.g.*, MX Hr'g Sl. (Ex. 25) at 52; '402 POR (Ex. 22) at 61-62. As explained above, this position requires that the toxicity of the marker be claimed subject matter. Second, also discussed above, Microspherix's IPR position that barium sulfate toxicity precludes a reasonable expectation of success in making the claimed invention was accepted by the panel. '402 FWD (Ex. 5) at 32. And third, it would be unfair for Microspherix to rely on a claim limitation to save validity, at which it succeeded as a matter of law, yet ignore that limitation when alleging infringement. Under Microspherix's current position that level of toxicity is not an implicit limitation, the PTAB would have found that Microspherix's arguments related to unclaimed subject matter. *Id.* at 25-26. It did not, indicating that level of toxicity is a limitation of the claims.

B. "radiopaque" / "radio-opaque"

Despite advancing in the IPRs the ***very same*** construction that Merck proposes

here, Microspherix no shifts course by proposing that for something to be radiopaque, it need only be "capable of visualization." Nothing in the specification supports a probabilistic understanding of whether something is radiopaque. Rather, "radiopaque" is used consistently in the specification to refer to something (e.g., material, strand, polymer, marker, or agent) that is detectable by x-ray. *See* '402 Patent at 2:26–44, 5:15–25, 10:25–26, 10:20–64, 18:17–21, 18:28–33, 18:56–19:9. Notably, throughout the IPRs and even in this litigation, Microspherix has taken positions that align with Merck's current construction—that is, the term "radiopaque" means something that absorbs or attenuates x-rays so that it is detectable by x-ray imaging. *See, e.g.*, [redacted] '402 POPR (Ex. 26) at 18 ("[T]he term radiopaque is used consistently throughout the specification **in only one manner** to refer to X-ray detectable materials."). The Court should thus adopt Merck's construction, which is taken word-for-word from the specification.

VII. CONCLUSION

Merck's proposed constructions comport with the claim language and intrinsic record as would be understood by a POSA, while Microspherix's proposed construction are incompatible with both. The Court should thus adopt Merck's proposed constructions.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on October 29, 2020, I caused a true and correct copy of Defendants' Opening Claim Construction Brief and supporting documents to filed on the Court's CM/ECF system, which will provide notice and constitutes service on all counsel of record. Copies of all documents filed, including those filed under seal, have been served on counsel or Plaintiffs by way of email.

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